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Seven-valent mKRAS-specific lymph node targeted amphiphile immunotherapy versus observation in resected pancreatic ductal adenocarcinoma (PDAC): The AMPLIFY-7P randomized phase 2 study

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Background

Resected PDAC harbors diverse KRAS mutations and high recurrence risk despite neoadjuvant/adjuvant therapy. Camupegimut (ELI-002 7P) induces mKRAS-specific T cell responses that correlated with Disease-Free and Overall Survival (DFS, OS) in phase 1. AMPLIFY-7P builds on promising signal.

Methods

AMPLIFY-7P is a randomized, open label phase 2 trial in patients (pts) with stages I-III, KRAS-mutated PDAC who received curative-intent therapy and no recurrence at ≤ 6 months. Pts randomized 2:1, stratified by lymph node status (N0 vs N1/2), to 10 doses camupegimut (prime, boost) or observation. Primary endpoint: investigator DFS; secondary: safety, 6-month DFS; success required Hazard Ratio (HR) ≤ 0.70, 2-sided alpha 0.10.

Results

From 01-12/2024, 144 pts with mKRAS PDAC; 44.4% G12D, 35.4% G12V, 16.7% G12R: randomized to camupegimut (n=96) or observation (n=48) at 24 centers. Stratification balanced nodal status (N1/N2: 57[59.4%] vs 29[60.4%]) but ctDNA(+) 20[20.8%] vs 6[12.5%]. Primary DFS endpoint not met (HR 0.85, p=0.539), however, pre-specified 6-month DFS advantage of 14% (75.7% vs 61.7%; HR=0.55; p=0.0557) and mKRAS-specific T cells correlated with efficacy (mDFS not reached vs 6.08 mo; HR=0.22; p<0.0001); subgroups promising DFS:.Table: LBA83

Subgroup	n(%)	DFS (mo)	HR	Nominal p
ctDNA(-)	93(65%)	NR vs 21.2	0.51	0.0280
No radiation	106(74%)	23.8 vs 10.4	0.59	0.0221

Post-hoc multivariate Cox regression analysis DFS: camupegimut adjusted HR=0.45; 95%CI 0.25-0.80; p=0.0064; ctDNA adjusted HR=6.72; 95%CI 3.49-12.94; p<0.0001. Grade ≥ 3 AEs (10.4 vs 14.6%); serious AEs (6.3 vs 8.3%); no new safety signals. Immunogenicity: mKRAS-specific T cell responses 99% (89/90); 85% (68/80) CD8+ and CD4+ T cells and antigen spreading 87% (13/15).

Conclusions

Prespecified 6-month subgroup DFS increased and DFS associated with mKRAS-specific T cell response, although primary DFS endpoint not met. Baseline ctDNA(+) adversely prognostic/imbalanced. Phase III planned with refined stratification and pt selection factors.

Clinical trial identification

NCT05726864.

Legal entity responsible for the study

Elicio Therapeutics.

Funding

Elicio Therapeutics.

Disclosure

E.M. O'Reilly: Financial Interests, Personal, Advisory Board, Travel reimbursement only: BioNTech, Pfizer; Financial Interests, Personal, Advisory Board, +Spouse: Ipsen; Financial Interests, Personal, Advisory Board: Merck, AstraZeneca, Novartis, Astellas, BMS, Exelixis, Agenus, Moma Therapeutics; Financial Interests, Personal, Advisory Board, Spouse: Genentech/Roche, Eisai, Autem; Financial Interests, Personal, Other, Data and Safety Monitoring Board: Ability Pharma; Financial Interests, Personal, Invited Speaker: Research To Practice; Financial Interests, Institutional, Local PI: Genentech/Roche, Arcus, Elicio, AstraZeneca, Tango Therapeutics; Financial Interests, Personal and Institutional, Coordinating PI: BioNTech; Financial Interests, Institutional, Coordinating PI: Pertzye; Financial Interests, Institutional, Research Grant: Parker Institute; Financial Interests, Personal and Institutional, Local PI, Consulting personal - uncompensated: Revolution Medicine; Financial Interests, Personal and Institutional, Local PI, Clinical trial Advisory Board: Agenus; Non-Financial Interests, Other, Scientific and Medical Advisory Board Uncompensated: Pancreas Cancer Action Network; Non-Financial Interests, Member of Board of Directors, Vice-Chair Uncompensated: National Pancreas Foundation; Non-Financial Interests, Other, Scientific advisory Board Uncompensated: Hirshberg Foundation; Other, Other, Editor: American Society of Clinical Oncology, American Association of Cancer Research (AACR); Other, Other, PI SPORE Grant to MSK (institution): NCI/NIH; Other, Other, Investigator on grant (to institution): BreakThroughCancer. 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But no financial implications yet.: Elicio Therapeutics; Financial Interests, Institutional, Research Grant, Grant support for MRD testing on our investigator initiated trial.: Haystack; Financial Interests, Institutional, Funding, PI of an investigator initiated trial.: Agenus; Financial Interests, Institutional, Other, Original sponsor investigator and current correlative chair of a multi center investigator initiated trial.: Merck, Novartis; Financial Interests, Institutional, Research Grant, PI of an investigator initiated trial and lead PI of an industry sponsored trial.: Cytodyn. G. Amato: Financial Interests, Personal, Full or part-time Employment: Elicio Therapeutics. L. McNeil: Financial Interests, Personal,

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